

General

Guideline Title

Panobinostat for treating multiple myeloma after at least 2 previous treatments.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Panobinostat for treating multiple myeloma after at least 2 previous treatments. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 27. 30 p. (Technology appraisal guidance; no. 380).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Panobinostat in combination with bortezomib and dexamethasone is recommended, within its marketing authorisation, as an option for treating multiple myeloma, that is, for 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent' when the company provides panobinostat with the discount agreed in the patient access scheme.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Multiple myeloma

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Hematology

Oncology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of panobinostat for treating multiple myeloma after at least 2 previous treatments

Target Population

Adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent

Interventions and Practices Considered

Panobinostat in combination with bortezomib and dexamethasone

Major Outcomes Considered

- Clinical effectiveness
 - Progression-free survival (PFS)
 - Response (complete response [CR], near-complete response [nCR], duration of response, time to response)
 - Overall survival (OS)
 - Health-related quality of life
 - Adverse effects of treatment
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Optimity Advisors and Peninsula Technology Assessment Group (PenTAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Company's Search Strategy and Comment on Whether the Search Strategy Was Appropriate

The company presented a literature search protocol to support its review of clinical effectiveness. This protocol included systematic searches of key biomedical databases using a literature search strategy and hand searching of conference abstracts. The literature searching was last updated in December 2014.

The bibliographic searching used a search strategy that took the following form:

1. (terms for myeloma) AND
2. (terms for relapse or indicative terms for failure at first line) AND
3. (terms for thalidomide or bortezomib or lenalidomide or pomalidomide or carfilzomib or ixazomib or panobinostat)

A limit to phase 2, phase 3, and phase 4 trials, and a limitation to randomised controlled trials (RCTs), was used. A limit to studies published in English language was applied and the searches were date limited 2003-December 2014.

The search strategy was applied in the following bibliographic databases: MEDLINE (OVID) and EMBASE (OVID). A simplified search strategy, consisting of database indexing terms for multiple myeloma and free text terms for relapsed or refractory, was used in The Cochrane Library (Central Register of Controlled Trials [CENTRAL], National Health Service Economic Evaluation Database [NHS EED], Database of Abstracts of Reviews of Effects [DARE], Cochrane Database of Systematic Reviews [CDSR] and the Health Technology Assessment [HTA] Library) in the first instance, and this was later supplemented with a search using controlled indexing terms for multiple myeloma. See the ERG report for the list of conference proceedings searched from 2011 to May 2014.

Within the submission, the company observes the paucity of mature trial data and is aware of further data that is now available to them. In view of additional data being available, and in reference to the submitted literature searches being over six months out of date, the ERG asked the company to update their literature searches. The company declined to do so.

In principal, the search syntax and search protocol was adequate to meet the requirements of this submission. However, the literature searches are now seven months old.

Indirect and Mixed Treatment Comparisons

Separate searches for indirect and/or mixed treatment comparators were not undertaken for this submission. The ERG notes however that the range of comparators used in the literature searching is broader than required in the scope.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection and Comment on Whether They Were Appropriate

Eligibility Criteria Used of Study Selection – June 2013

Clinical Effectiveness	Inclusion Criteria	Exclusion Criteria
Populations	Relapsed/refractory MM	Nonrelapsed/nonrefractory MM
Interventions	<ul style="list-style-type: none">• Bortezomib• Carfilzomib• Lenalidomide• Panobinostat• Pomalidomide• Thalidomide• Ixazomib	<ol style="list-style-type: none">1. Induction or maintenance therapy or other combinations of therapy, i.e., results were reported for a sequence of therapy rather than a single regimen2. Treatment of interest is the focus of the study, i.e., studies of the treatment of interest in conjunction with a new treatment are not included.
Outcomes	<ul style="list-style-type: none">• Response rate: CR and CR+VGPR+PR	Analysis of prognostic factors

Clinical Effectiveness	Inclusion Criteria	Exclusion Criteria
	<ul style="list-style-type: none"> TTP OS 	
Study Design	<ul style="list-style-type: none"> Clinical trials or RCT Phase II clinical trial Phase III clinical trial Phase IV clinical trial 	<ol style="list-style-type: none"> Phase I/II studies unless they specifically reported results for phase II of the study Retrospective studies
Publication Type	Report of primary data	Review, editorial, letter, or secondary publication
Language Restrictions	English	Non-English languages

Abbreviations: CR, complete response; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PR, partial response; RCT, randomised controlled trial; TTP, time to progression; VGPR, very good partial response.

The ERG noticed that progression-free survival (PFS) was not included in the initial search. The company does not provide a rationale why PFS was omitted from the initial search. PFS is included in the update searches.

Eligibility Criteria Used in Study Selection – April and December 2014 Review

Clinical Effectiveness	Inclusion Criteria	Exclusion Criteria
Populations	Patients with relapsed/refractory MM	<ul style="list-style-type: none"> Non-relapsed/non-refractory multiple myeloma Animal/in vitro studies
Interventions	<ul style="list-style-type: none"> Panobinostat/LBH-589 Thalidomide/K-17 Bortezomib/MG-341/PS-341 Lenalidomide/CC-5013 Pomalidomide/CC-5013 Carfilzomib/PR-171 Ixazomib/MLN-9708 Elotuzumab/HuLuc63 Vorinostat/Zolinza Daratumumab/HuMax-CD38 Dexamethasone* 	<ol style="list-style-type: none"> Induction or maintenance therapy or other combinations of therapy, i.e., results were reported for a sequence of therapy rather than a single regimen. Treatment of interest is the focus of the study, i.e., studies of the treatment of interest in conjunction with a new treatment are not included.
Study Design	<ul style="list-style-type: none"> Single- or double-blinded RCTs Non-RCTs Phase II clinical trial Phase III clinical trial Phase IV clinical trial Long term follow-up studies (e.g., open-label studies) 	<ul style="list-style-type: none"> Pharma-sponsored database analyses (except if conducted by Novartis) Pre-clinical and phase I studies Prognostic studies Case reports Editorials, commentaries and letters General reviews Systematic reviews and meta-analyses Pharmacodynamic studies Retrospective studies
Outcomes	<ul style="list-style-type: none"> Response rate: CR and CR+VGPR+PR TTP/PFS OS 	<ul style="list-style-type: none"> No relevant data on outcomes of interest Analysis of prognostic factors
Publication	<ul style="list-style-type: none"> English language Published from January 2013 to April 2014 	<ul style="list-style-type: none"> Non-English language Published pre-2013 Editorial

Clinical Effectiveness	Inclusion Criteria	Exclusion Criteria
		<ul style="list-style-type: none"> • Review • Letter • Reference included in original systematic review

*Dexamethasone to be captured only when used in combination with an intervention named above.

Abbreviations: CR, complete response; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PR, partial response; RCT, randomised controlled trial; TTP, time to progression; VGPR, very good partial response.

Overall these criteria seem appropriate to identify all relevant evidence on the clinical effectiveness of panobinostat (PANO). Despite this, the ERG requested clarification on some aspects of the search.

The manufacturer's submission includes flow diagrams that show the number of studies identified through the database searches and the number of studies included and excluded at each stage of the review and the reasons for exclusion. After the ERG requested clarification, the number of excluded studies in the first systematic review that took place in June 2013 was corrected from 87 to 386.

Only one study was identified for direct comparison.

In addition, indirect and mixed comparisons were conducted.

The search strategy identified 3 references in the final search: 1 full paper and 2 abstracts. Only the full paper (PANORAMA-1) was deemed appropriate for the company for inclusion. The company does not give any more details on the 2 abstracts. No details of excluded papers are presented.

Economic Evaluation

Description of Company's Search Strategy and Comment on Whether the Search Strategy Was Appropriate

The company presented a literature search protocol to support its review of cost-effectiveness. This protocol included systematic searches of key biomedical databases using a literature search strategy and hand searching of conference abstracts. The search protocol was last updated in December 2014.

Two literature searches were run using slightly different syntax structures:

Search one (2006 – August 2013) took the following form:

1. (terms for myeloma) AND
2. (a study design search filter for costs or economic data)

Search two (April 2013 – April 2014 and then April 2014 – December 2014) took the following form:

1. (terms for myeloma) AND
2. (terms/a study design search filter for costs or economic data) AND
3. (terms for thalidomide or bortezomib or lenalidomide or pomalidomide or carfilzomib or ixazomib or panobinostat)

Literature searching for published studies was conducted in MEDLINE, MEDLINE in Process and EMBASE all via OVID. See the ERG report for the list of conference proceedings searched from 2011 to May 2014.

A limit to studies published in the English language was applied and the searches were limited by date. A different date parameter was used on these searches (2006 – December 2014) compared with the review of clinical effectiveness (which used 2003 – December 2014). The inclusion criteria used in the screening is presented in Table 36 in the ERG report.

The ERG is content with the searches for this element of the submission.

Search Results

The ERG are concerned as no PRISMA (preferred reporting items for systematic reviews and meta-analysis) is presented for cost-effectiveness searches; it is not possible to tell how many studies were identified through searches or excluded.

The company states their systematic review identified 14 cost-utility studies; however, only seven studies were reviewed in detail in full papers or HTA submissions and were presented (see Table 37 in the ERG report). No description of these studies is presented by the company. The ERG summarises these studies only in the table. In addition, the company states that construction of the economic model was informed by the review of

the previous modelling approaches. The ERG was not clear whether the company was referring to separate searches or these seven studies were identified by the systematic review mentioned above. However, when the ERG reviewed Appendix 17 of the manufacturer's submission (see the "Availability of Companion Documents" field) where the subgroup analysis is performed, the ERG found that a targeted literature search was performed to identify previously published pharmacoeconomic models and HTA submissions. The ERG assumes that the company was referring to the targeted literature review; however, it is not clear from the submission.

The company only presented the table with the summary of 7 studies. It is not clear to the ERG why the remaining 7 studies were omitted from the submission.

Number of Source Documents

Clinical Effectiveness

- One randomised controlled trial (RCT, PANORAMA-1) was included in the review.
- Two published non-RCTs were presented to provide evidence for the efficacy and safety of panobinostat (PANO) in combination with bortezomib/dexamethasone (BTZ/DEX) relative to BTZ/DEX.

Economic Evaluation

- The manufacturer states their systematic review identified 14 cost-utility studies; however, only seven studies were reviewed in detail in full papers or Health Technology Assessment (HTA) submissions.
- The manufacturer submitted an economic model and subgroup analysis.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Optimity Advisors and Peninsula Technology Assessment Group (PenTAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of Company Approach to Validity Assessment

One study presented in the company submission is assessed for validity. Table 9 in the ERG report provides the quality assessment of study PANORAMA-1.

Indirect and Mixed Treatment Comparison

Since there was no evidence which allowed a direct comparison between panobinostat/bortezomib/dexamethasone (PANO/BTZ/DEX) and lenalidomide (LEN)/DEX, the company undertook an indirect treatment comparison in order to estimate the relative effectiveness between those two treatments.

The company included 5 studies in the analysis. However, it is not very clear to the ERG how these five studies were identified.

These studies were said to be similar in design such as patient selection criteria. The patient characteristics were similar in terms of median age, disease duration, proportion of patients with 1 prior line of therapy, "except for the matched pairs analysis, where only patients with one prior line of therapy were considered." In total 3005 patients were included in the studies. The evidence network for the common comparator method is presented in Figure 18 of the ERG report.

Statistical assessment of heterogeneity was not conducted as there was only one trial per treatment except for LEN/DEX which had two different trials MM-009 and MM-010. An assessment of heterogeneity could have been conducted. The ERG notes that both trials were used as pooled data to provide data for LEN/DEX vs. DEX. However, it should be noted that the MM-009 population was mainly enrolled from sites in the USA and Canada. Therefore some population characteristics (like ethnicity) are potentially different from the average UK population. MM-010 enrolled patients mainly from Europe; hence, this typically reflects the UK population in a better fashion.

Description and Critique of the Methods and Outcomes of Included Studies

Four different methodologies were used for indirect treatment comparisons although the company states that three methods were used. The summary of the used methods is presented in Table 21 of the ERG report.

Common Comparators Method

As described in the submission, this method relies on the randomisation within each trial that compared the treatment directly and using the relative effect measures for analysis. This method thus separates the true efficacy of a drug from possible placebo effects.

The fixed-effects models were used to estimate hazard ratio of progression-free survival (PFS), time to progression (TTP), and overall survival (OS); and the odds ratios of complete response/near-complete response (CR/nCR).

The summary of data used in common comparators method is summarised in Table 22 of the ERG report.

Refer to Section 4 of the ERG report for additional information on clinical effectiveness analysis.

Economic Evaluation

The Company's Economic Model Submitted to NICE

The company reports cost per quality-adjusted life year (QALY) estimates for PANO/BTZ/DEX vs. BTZ/DEX for the full cohort included in the PANORAMA-1 trial which enrolled patients with relapsed or relapsed and refractory multiple myeloma who had received one to three previous treatments. The model was built in Microsoft Excel®.

Model Structure

The company developed a decision analytic semi-Markov model. The structure of the model, illustrated in Figure 23 of the ERG report, includes two pre-progression health states, two post-progression health states and finally the death health state. The model is reported to capture the three key aspects of multiple myeloma that are affected by disease progression and the effects of treatment, namely survival, health-related quality of life (HRQL) and costs.

All patients enter the model in the pre-progression health state A and receive either PANO/BTZ/DEX or BTZ/DEX. Patients progress by moving from the two pre-progression health states, A and B, to the post-progression health state C (LEN/DEX) and then D corresponding to fourth-line therapy (POM/DEX together with supportive care).

Patients in the PANO/BTZ/DEX treatment arm discontinue early due to progression or relapse and move to C, or discontinue due to reasons other than progression and move to B. Patients who discontinue treatment due to progression or relapse or have not achieved a partial remission (PR) will move to C, while those who discontinue due to reasons other than progression and have at least a PR stop treatment and remain off treatment in B, until they experience progression and move to C. Following progression, patients will move to D until death.

The cycle length in the economic model is three weeks to reflect the drug administration schedule in PANORMA-1 trial and a half-cycle correction was applied.

The time horizon considered in the economic model was 25 years.

Refer to Section 5 of the ERG report for additional information on economic evaluation submitted by the company and the critique of company's approach by ERG. See also Section 6 of the ERG report for information on subgroup analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an Assessment Report. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee considered the company's new models and cost-effective analyses which were submitted as a response to the appraisal consultation document and the Evidence Review Group's (ERG) critique for the comparison of panobinostat plus bortezomib and dexamethasone with lenalidomide plus dexamethasone.

The Committee recalled that the PANORAMA-1 trial provided trial data for this comparison in the population included in the marketing

authorisation for panobinostat. However, the Committee considered that this analysis was not required for its decision making because the company had provided a new indirect comparison with the relevant comparator (lenalidomide plus dexamethasone). The Committee therefore considered that bortezomib plus dexamethasone was not the appropriate comparator and agreed not to consider this comparison further.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee considered the company's method for applying the time-dependent hazard ratios for progression-free and overall survival (OS) from the matching adjusted indirect treatment comparison.

The Committee questioned the face validity of both the calculated quality-adjusted life year (QALY) gains and the calculated cost differences after treatment discontinuation. It noted that the QALY advantage for panobinostat occurred after treatment discontinuation. The Committee also noted that the costs in the post-progression health state were lower for panobinostat plus bortezomib and dexamethasone than for lenalidomide plus dexamethasone, even though panobinostat was an additional component to the comparator regimen. The company explained that the post-progression state analyses took into account the different percentage of people who had subsequent treatment in the PANORAMA-1 trial. The company further explained that the subsequent treatments provided in the trial were not all standard treatments in clinical practice in the UK and therefore it adjusted the treatments to reflect clinical practice in the UK. The Committee was aware that in its new analyses, the company had removed the costs of subsequent treatment but had not adjusted the clinical effectiveness.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee noted that the company had measured health-related quality of life in the PANORAMA-1 trial to provide utility values for the pre-progression with panobinostat treatment health state. The Committee also noted that disutilities had not been incorporated in the model. However, because health-related quality of life data were collected in the PANORAMA-1 trial, these values would have included chronic adverse events.

The Committee also noted that EuroQol 5-Dimension (EQ-5D) data were not available for lenalidomide plus dexamethasone and that the company used 2 scenarios for the utility value for pre-progression patients having lenalidomide. The Committee concluded that the utility values used by the company were appropriate.

The Committee concluded that there were no additional gains in health-related quality of life over those already included in the QALY calculations, and that there was no need to change its conclusions on that basis.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

Not applicable

What Are the Key Drivers of Cost-effectiveness?

The Committee discussed the costs included in the model, particularly the administration costs of bortezomib. The Committee heard from the clinical experts that almost all patients have bortezomib by subcutaneous administration and so it concluded this to be the most appropriate bortezomib cost to be included in the model.

The Committee considered how the company applied time-dependent hazard ratios for progression-free survival (PFS) and OS from the matching adjusted indirect treatment comparison in the economic model and noted the curves were fitted only based on predictors of survival. The Committee noted that the company had used a Weibull distribution for extrapolating the PFS data without also exploring exponential distribution. Nevertheless, the Committee concluded that the use of time-dependent hazard ratios based on the matching adjusted indirect comparison was acceptable in its decision-making.

The Committee noted that subsequent treatment (post-progression) data had not been published for lenalidomide plus dexamethasone, so the company assumed that patients in this treatment group received the subsequent treatments in similar proportions to those reported for bortezomib and dexamethasone in the PANORAMA-1 trial.

The Committee was aware that in its new analyses, the company had removed the costs of subsequent treatment but did not adjust the clinical effectiveness, causing a mismatch between the total costs and efficacy of panobinostat.

Most Likely Cost-effectiveness Estimate (Given as an Incremental Cost-effectiveness Ratio [ICER])

Considering all of the new evidence available for the comparison of panobinostat plus bortezomib and dexamethasone with lenalidomide plus dexamethasone, which included the updated patient access scheme, the Committee concluded that the ICER was likely to be no higher than £25,000 per QALY gained and therefore within the range that would normally be considered a cost-effective use of National Health Service

(NHS) resources.

Patient Access Schemes

The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of panobinostat, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of panobinostat and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from one randomised controlled trial (RCT). For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The Committee accepted that the results from the PANORAMA-1 trial used in the post hoc subgroup analysis demonstrated that panobinostat plus bortezomib and dexamethasone was clinically more effective than bortezomib plus dexamethasone based on the interim and final overall survival data.

Potential Harms

In the PANORAMA-1 trial, diarrhoea, thrombocytopenia, anaemia, fatigue and nausea occurred more often in patients receiving panobinostat plus bortezomib and dexamethasone than in patients receiving placebo plus bortezomib and dexamethasone.

Qualifying Statements

Qualifying Statements

- The recommendations in this guidance represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the National Health Service Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the [National Institute for Health and Care Excellence \(NICE\) \(Constitution and Functions\) and the Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has relapsed and/or refractory multiple myeloma and the doctor responsible for their care thinks that panobinostat is the right treatment, it should be available for use, in line with NICE's recommendations.
- The Department of Health and Novartis have agreed that panobinostat will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to the Novartis Commercial Operations team on 01276 698717 or commercial.team@novartis.com

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Panobinostat for treating multiple myeloma after at least 2 previous treatments. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 27. 30 p. (Technology appraisal guidance; no. 380).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jan 27

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download in ePub and eBook formats from the [NICE Web site](#) .

Availability of Companion Documents

The following are available:

- Panobinostat for treating multiple myeloma after at least 2 previous treatments. Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 6 p. (Technology appraisal guidance; no. 380). Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .
- Panobinostat for treating multiple myeloma after at least 2 previous treatments. Costing template. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. (Technology appraisal guidance; no. 380). Available from the [NICE Web site](#) .
- Durand A, Rtveldazde K, Pritchard C, Cooper C, Mujica-Mota R. The clinical and cost-effectiveness of panobinostat for treating multiple myeloma in people received at least one prior therapy. Single technology appraisal. London (UK): Optimity Advisors and Peninsula Technology Assessment Group (PenTAG); 2015 Jul. 183 p. Available from the [NICE Web site](#) .
- Panobinostat for treating multiple myeloma in people who have received at least one prior therapy (ID663). Single technology appraisal. Manufacturer's submission. Novartis; 2015. 231 p. Available from the [NICE Web site](#) .

Patient Resources

The following is available:

- Panobinostat for treating multiple myeloma after at least 2 previous treatments. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 3 p. (Technology appraisal guidance; no. 380). Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download in ePub and eBook formats from the [NICE Web site](#) . Also available in Welsh from the [NICE Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on April 14, 2016.

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